U.S. CLAIMS

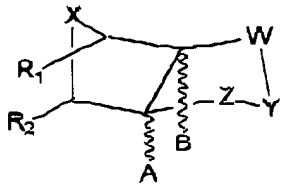
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. A cell permeable inhibitor of protein phosphatase, said inhibitor being an anhydride modified cantharidin analogue.

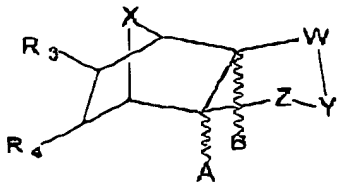
2. An inhibitor according to claim 1, wherein the phosphatase is phosphatase 1 and/or phosphatase 2A.

3. An inhibitor according to claim 1 or 2 wherein the anhydride modified cantharidin analogue is oxidatively stable.

4. A compound of the formula:



wherein R_1 and R_2 are H, aryl or alkyl; X is O, N or S; Y is O, S, SR, NH, NR, CH_2OH, CH_2OR; R is alkyl or aryl; A and B are H or CH_3; W and Z are CHOH or C=0 and R_1 and R_2 can cyclise to form a ring as follows:



wherein R_3 and R_4 are H, aryl or alkyl.

5. A compound according to claim 3, wherein the aryl group is phenyl or naphthyl and wherein the aryl group is attached via a carbon spacer of between 6 and 10 carbon atoms.

6. A compound according to claim 3 or claim 4, wherein the alkyl group is C_1-C_{10}.

7. A process for producing anhydride modified cantharidin analogues for use in the treatment of cancer or for the sensitising cancer cells to one or more cancer treatments comprising the step of reacting a diene with an ene.

8. A process according to claim 7 further comprising hydrogenation of the adduct of the diene and the ene.

9. A process according to claim 7 further comprising ring opening of the adduct of the diene and the ene.

10. A process for producing anhydride modified cantharidin analogues, said process including the steps of:

dissolving a diene in a suitable solvent and adding to the resultant solution an ene.

11. A process for producing anhydride modified cantharidin analogue, said process including the steps of:

dissolving a furan in a suitable solvent and adding to the resultant solution an ene;

incubating the solution at a temperature and for a time sufficient to form a precipitate; and

collecting the precipitate and recrystalising the analogue.

12. A process for producing anhydride modified cantharidin analogue, said process including the steps of:

mixing thiophene and maleic anhydride at room temperature in a suitable solvent;

compressing the mixture at a temperature and pressure sufficient to facilitate a reaction to take place; and

purifying the analogue.

13. A method of treating cancer which method comprises administering to a patient in need of such treatment, an effective amount of an inhibitor according to claim 1 or a compound according to claim 4, together with a pharmaceutically acceptable carrier, diluent and/or excipient.

14. A method according to claim 13, wherein the cancer is inherently resistant to conventional chemotherapy.

15. A method according to claim 13, wherein the cancer is colon cancer or non small-cell lung cancer.

16. A method according to claim 13, wherein the inhibitor or the compound is administered intravenously.

17. A method of sensitising cancer cells to at least one method of treating cancer, which method of sensitising comprises administering to a patient in need of such treatment, an effective amount of an inhibitor according to claim 1 or a compound according to claim 4, together with a pharmaceutically acceptable carrier, diluent and/or excipient.

18. A method according to claim 17, wherein the at least one cancer treatment is selected from treatments involving irradiation and anti-cancer agents.

19. A method according to claim 17, wherein the cells have deficient p53 activity.

20. A method of treating cancer which method comprises:

administering to a patient in need of such treatment, an effective amount of an anhydride modified cantharidin analogue of claim 1 or a compound according to claim 4 to sensitise cells of the patient to one or more cancer treatments; and

utilising the one or more cancer treatments.

21. A method of screening compounds for use in sensitising cancer cells to at least one method of treating cancer, and comprising:

screening for anti-cancer activity; and

screening for ability to abrogate either the G_1 or the G_2 checkpoint of the cancer cell cycle.

22. A method according to claim 21 further comprising the step of screening for the ability of the compounds of sensitise cancer cells to one or more cancer treatments.

23. A method according to claim 21 wherein the one or more cancer treatments are selected from treatments involving cisplatin, irradiation, taxanes and antimetabolites.

24. A method according to claim 21 wherein the screening is conducted on haematopoietic cells or solid tumour cells, having varying p53 activity.

25. A method according to claim 24, wherein the cells are selected form the group consisting of L1210 (murine leukaemia, p53 wildtype), HL60 (human leukaemia, p53 nul), A2780 (human ovarian carcinoma, p53 wildtype), ADDP (cisplatin resistant A2780 cells, p53 mutant), SW480 (human colon carcinoma, p53 mutant), WiDr (human colon carcinoma, p53 mutant), HT29 (human colon carcinoma, p53 mutant), HCT116 (human colon carcinoma, p53 wildtype) and 143B (human osteosarcoma, p53 mutant).

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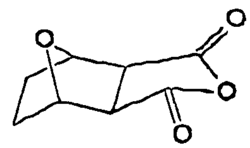
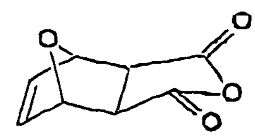
26. A compound selected from a group comprising compounds (a) to (n) below:

(a)



(b)



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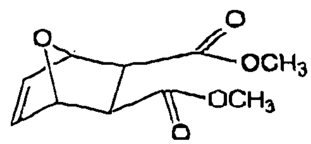
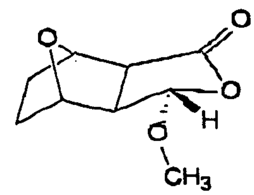


(d)



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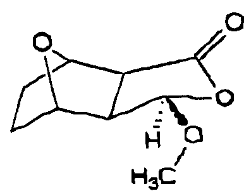

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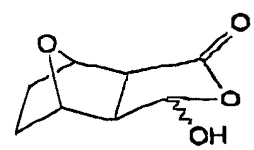
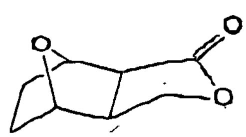


(g)



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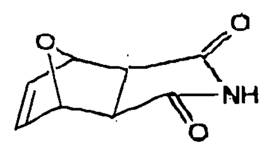
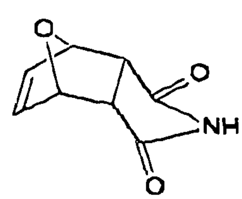


(i)



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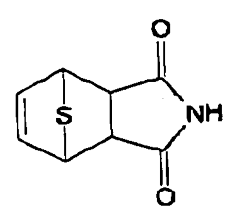

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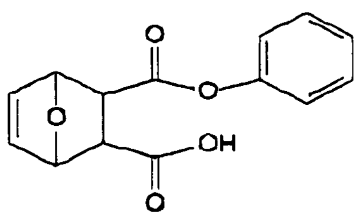
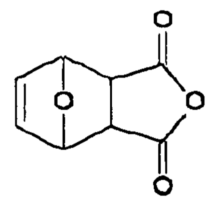
(k)



(l)



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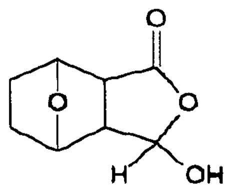

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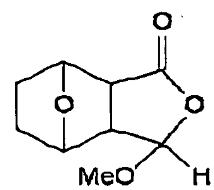

27. Use of an inhibitor according to claim 1, or a compound according to claim 4 for the manufacture of a medicament for the treatment of cancer.

28. Use according to claim 27, wherein the cancer is colon cancer or non small-cell lung cancer.

29. Use according to claim 28, wherein the medicament is administered intravenously.

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